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L* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:32:09 ON 23 SEP 2008

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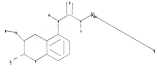
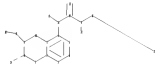




chain nodes :
11 12 13 14 15 16 17 19 21 22 23
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
4-13 8-19 9-11 11-12 13-14 13-23 14-15 14-21 15-16 15-22 16-17
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10
exact/norm bonds :
2-7 3-10 4-13 7-8 8-9 8-19 9-10 9-11 13-14 14-15 14-21 16-17
exact bonds :

11-12 13-23 15-16 15-22
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

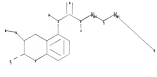
G1:H,O

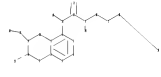
G2:O,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 19:CLASS
21:CLASS 22:CLASS 23:CLASS

L1 STRUCTURE UPLOADED

=>
Uploading C:\Program Files\Stnexp\Queries\10578413.str





chain nodes :
11 12 13 14 15 16 17 18 19 21 23 24 25
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :

4-13 8-21 9-11 11-12 13-14 13-25 14-15 14-23 15-16 15-24 16-17 17-18
18-19
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10
exact/norm bonds :
2-7 3-10 4-13 7-8 8-9 8-21 9-10 9-11 13-14 14-15 14-23 16-17 17-18
18-19
exact bonds :
11-12 13-25 15-16 15-24
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

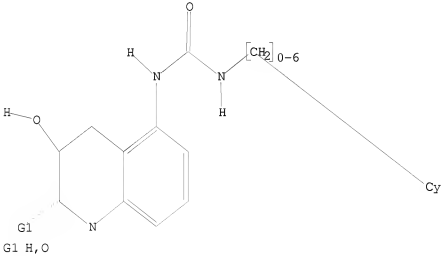
G1:H,O

G2:O,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:Atom 21:CLASS 23:CLASS 24:CLASS 25:CLASS

L2 STRUCTURE UPLOADED

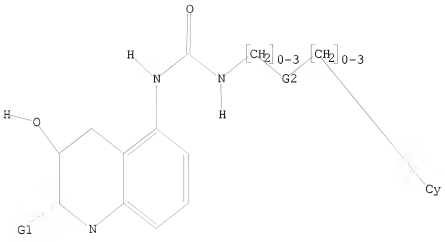
=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 H,O
G2 O,N

Structure attributes must be viewed using STN Express query preparation.

=> d l2
L2 HAS NO ANSWERS
L2 STR



G1 H,O

G2 O,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1 or l2 full
L5 29 SEA SSS FUL L1 OR L2

=> file ca

=> s l5
L6 2 L5

=> d ibib abs hitstr 1-2

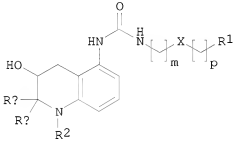
L6 ANSWER 1 OF 2 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 142:463618 CA
TITLE: Preparation of 1,2,3,4-tetrahydroquinolinylurea derivatives as vanilloid receptor antagonists
INVENTOR(S): Bouchon, Axel; Diedrichs, Nicole; Hermann, Achim; Lustig, Klemens; Meier, Heinrich; Pernerstorfer, Josef; Reissmueller, Elke; Mogi, Muneto; Fujishima, Hiroshi; Tajimi, Masaomi; Yamamoto, Noriyuki
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2005044802	A2	20050519	WO 2004-EP12051		20041026
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2545109	A1	20050519	CA 2004-2545109		20041026
EP 1685112	A2	20060802	EP 2004-790836		20041026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
JP 2007523888	T	20070823	JP 2006-538691		20041026
US 20070213363	A1	20070913	US 2006-578413		20060505
PRIORITY APPLN. INFO.:			EP 2003-25575	A	20031108
			WO 2004-EP12051	W	20041026

OTHER SOURCE(S): CASREACT 142:463618; MARPAT 142:463618

GI



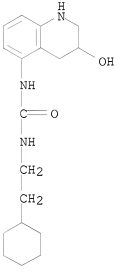
I

AB This invention relates to 1,2,3,4-tetrahydroquinolinylurea derivs. (I) and salts thereof [wherein m, p = 0-3; X = bond, O, N(R10) (wherein R10 = H, C1-6 alkyl); with the proviso that when m = 0, then X = a bond; RA = RB = H, or RA and RB together form a carbonylgroup with the carbon-atom to which they are connected; R1 = each (un)substituted aryl or heteroaryl; R2 = C1-6 alkylcarbonyl, C1-6 alkylsulfonyl, H, HO, aryl, heteroaryl, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, arylsulfonyl, or heteroaryl sulfonyl, wherein said alkyl, alkenyl or alkynyl are optionally substituted] which are useful as active ingredients of pharmaceutical prepns. The 1,2,3,4-tetrahydroquinolinylurea derivs. of the present invention have vanilloid receptor (VR1) antagonistic activity (no data). These compds. can be used for the prophylaxis and treatment of diseases associated with VR1 activity, in particular for the treatment of urol. diseases or disorders, such as detrusor overactivity (overactive bladder), urinary incontinence, neurogenic detrusor overactivity (detrusor hyperflexia), idiopathic detrusor overactivity (detrusor instability), benign prostatic hyperplasia, and lower urinary tract symptoms; pain such as chronic pain, neuropathic pain, postoperative pain, rheumatoid arthritic pain, neuralgia, neuropathies, algesia, nerve injury, ischemia,

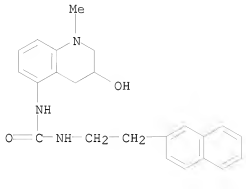
neurodegeneration, and stroke; and inflammatory disorders such as asthma and chronic obstructive pulmonary (or airways) disease (COPD). Thus, 5-amino-3-hydroxy-3,4-dihydroquinolin-2(1H)-one > (300 mg, 1.68 mmol) was dissolved in EtOAc and cooled to 0° and 4-trifluoromethylbenzyl isocyanate (339 mg, 1.68 mmol) was added slowly with stirring. The reaction mixture was stirred for 1 h at room temperature and the insol. product was filtered and dried in vacuo to give 16% N-(3-Hydroxy-2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)-N'-[4-(trifluoromethyl)benzyl]urea (103 mg).

IT 1043481-45-3 1043481-49-7 1043481-50-0
1043481-57-7 1043481-58-8 1043481-71-5
1043481-72-6 1043481-80-6 1043481-82-8
1043481-93-1 1043481-94-2 1043481-98-6
1043481-99-7 1043482-08-1 1043482-09-2
1043482-12-7 1043482-20-7 1043482-21-8
1043482-22-9 1043482-24-1 1043482-38-7
RL: PRPH (Prophetic)
(Preparation of 1,2,3,4-tetrahydroquinolinylurea derivatives as vanilloid receptor antagonists)

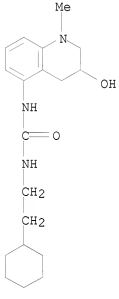
RN 1043481-45-3 CA
CN Urea, N-(2-cyclohexylethyl)-N'-(1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)



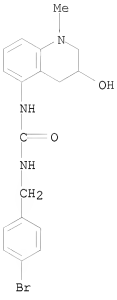
RN 1043481-49-7 CA
CN Urea, N-[2-(2-naphthalenyl)ethyl]-N'-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)- (CA INDEX NAME)



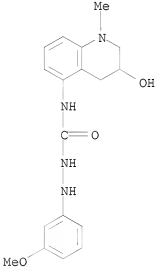
RN 1043481-50-0 CA
CN Urea, N-(2-cyclohexylethyl)-N'-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)- (CA INDEX NAME)



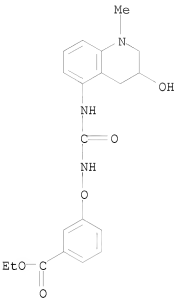
RN 1043481-57-7 CA
CN Urea, N-[(4-bromophenyl)methyl]-N'-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)- (CA INDEX NAME)



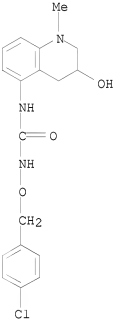
RN 1043481-58-8 CA
CN Hydrazinecarboxamide, 2-(3-methoxyphenyl)-N-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)- (CA INDEX NAME)



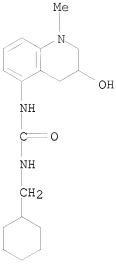
RN 1043481-71-5 CA
CN INDEX NAME NOT YET ASSIGNED



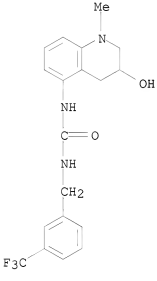
RN 1043481-72-6 CA
CN Urea, N-[(4-chlorophenyl)methoxy]-N'-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)- (CA INDEX NAME)



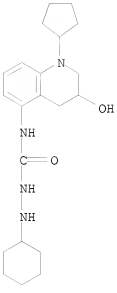
RN 1043481-80-6 CA
CN Urea, N-(cyclohexylmethyl)-N'-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)- (CA INDEX NAME)



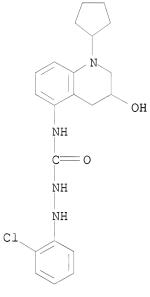
RN 1043481-82-8 CA
CN Urea, N-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)-N'-[[3-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)



RN 1043481-93-1 CA
CN Hydrazinecarboxamide, 2-cyclohexyl-N-(1-cyclopentyl-1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)

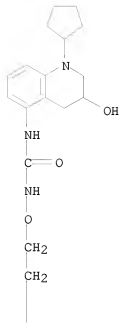


RN 1043481-94-2 CA
CN Hydrazinecarboxamide, 2-(2-chlorophenyl)-N-(1-cyclopentyl-1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)



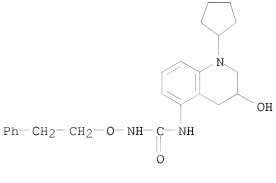
RN 1043481-98-6 CA
CN Urea, N-[2-(4-bromophenyl)ethoxy]-N'-(1-cyclopentyl-1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)

PAGE 1-A



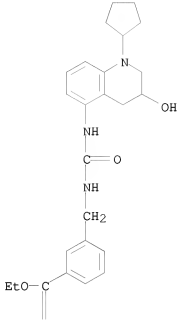
PAGE 2-A

RN 1043481-99-7 CA
CN Urea, N-(1-cyclopentyl-1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)-N'-(2-phenylethoxy)- (CA INDEX NAME)



RN 1043482-08-1 CA
CN Benzoic acid, 3-[[[[(1-cyclopentyl-1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)amino]carbonyl]amino]methyl]-, ethyl ester (CA INDEX NAME)

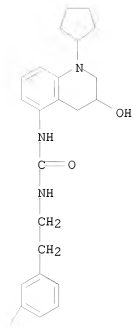
PAGE 1-A



PAGE 2-A

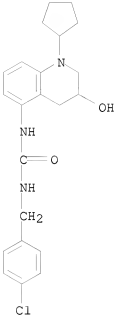
RN 1043482-09-2 CA
CN Urea, N-(1-cyclopentyl-1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)-N'-[2-[3-(trifluoromethyl)phenyl]ethyl]- (CA INDEX NAME)

PAGE 1-A

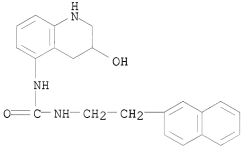


PAGE 2-A

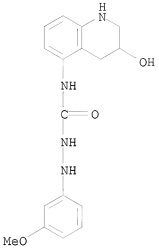
RN 1043482-12-7 CA
CN Urea, N-[(4-chlorophenyl)methyl]-N'-(1-cyclopentyl-1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)



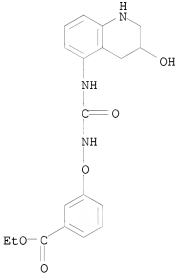
RN 1043482-20-7 CA
CN Urea, N-[2-(2-naphthalenyl)ethyl]-N'-(1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)



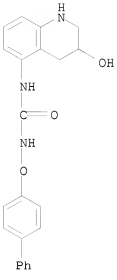
RN 1043482-21-8 CA
CN Hydrazinecarboxamide, 2-(3-methoxyphenyl)-N-(1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)



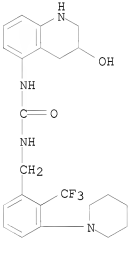
RN 1043482-22-9 CA
CN INDEX NAME NOT YET ASSIGNED



RN 1043482-24-1 CA
CN Urea, N-([1,1'-biphenyl]-4-yloxy)-N'-(1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)



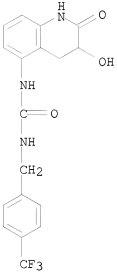
RN 1043482-38-7 CA
CN Urea, N-[[3-(1-piperidinyl)-2-(trifluoromethyl)phenyl]methyl]-N'-(1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)



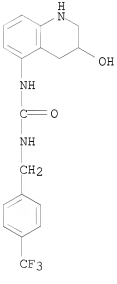
IT 851786-30-6P, N-(3-Hydroxy-2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)-N'-[4-(trifluoromethyl)benzyl]urea 851786-31-7P, N-(3-Hydroxy-1,2,3,4-tetrahydroquinolin-5-yl)-N'-[4-(trifluoromethyl)benzyl]urea 851786-32-8P, N-(4-Chlorophenyl)-N'-(3-hydroxy-1-methyl-1,2,3,4-tetrahydroquinolin-5-yl)urea 851786-33-9P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-hydroxy-1-methyl-1,2,3,4-tetrahydroquinolin-5-yl)urea 851786-34-0P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-hydroxy-1,2,3,4-tetrahydroquinolin-5-yl)urea 851786-35-1P, Ethyl 3-[[[(3-hydroxy-1-methyl-1,2,3,4-tetrahydroquinolin-5-yl)amino]carbonyl]amino]benzoate 851786-36-2P, N-(Biphenyl-3-yl)-N'-(3-hydroxy-1-methyl-1,2,3,4-tetrahydroquinolin-5-

yl)urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tetrahydroquinolinylurea derivs. as vanilloid receptor VR1 antagonists)

RN 851786-30-6 CA
CN Urea, N-(1,2,3,4-tetrahydro-3-hydroxy-2-oxo-5-quinolinyl)-N'-[[4-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)

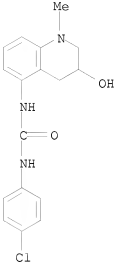


RN 851786-31-7 CA
CN Urea, N-(1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)-N'-[[4-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)

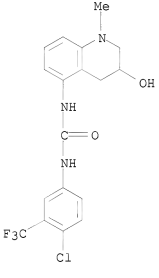


RN 851786-32-8 CA

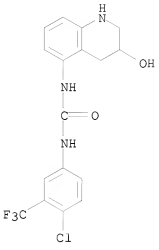
CN Urea, N-(4-chlorophenyl)-N'-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)- (CA INDEX NAME)



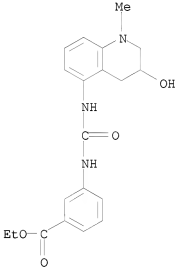
RN 851786-33-9 CA
CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)- (CA INDEX NAME)



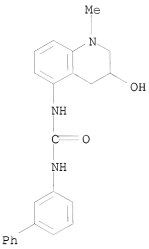
RN 851786-34-0 CA
CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-(1,2,3,4-tetrahydro-3-hydroxy-5-quinolinyl)- (CA INDEX NAME)



RN 851786-35-1 CA
CN Benzoic acid, 3-[[[(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)amino]carbonyl]amino]-, ethyl ester (CA INDEX NAME)



RN 851786-36-2 CA
CN Urea, N-[1,1'-biphenyl]-3-yl-N'-(1,2,3,4-tetrahydro-3-hydroxy-1-methyl-5-quinolinyl)- (CA INDEX NAME)



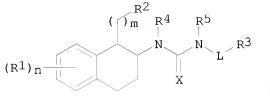
L6 ANSWER 2 OF 2 CA COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 140:4865 CA
TITLE: Aminotetralin-derived urea modulators of vanilloid VR1 receptor useful for treatment of pain, inflammation, etc.
INVENTOR(S): Codd, Ellen; Dax, Scott L.; Jetter, Michele; Mcdonell, Mark; Mcnally, James J.; Youngman, Mark
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097586	A1	20031127	WO 2003-US15254	20030515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2486092	A1	20031127	CA 2003-2486092	20030515
AU 2003241453	A1	20031202	AU 2003-241453	20030515
US 20030236280	A1	20031225	US 2003-438477	20030515
US 6984647	B2	20060110		
EP 1506166	A1	20050216	EP 2003-731189	20030515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005526137	T	20050902	JP 2004-505319	20030515

US 20050187291	A1	20050825	US 2005-45956		20050128
US 20080097102	A1	20080424	US 2007-877220		20071023
PRIORITY APPLN. INFO.:			US 2002-381575P	P	20020517
			US 2003-438477	A3	20030515
			WO 2003-US15254	W	20030515
			US 2005-45956	A1	20050128

OTHER SOURCE(S): MARPAT 140:4865

GI



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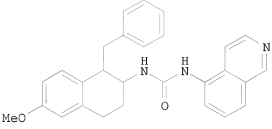


II

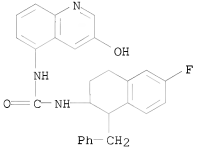
AB The invention is directed to vanilloid receptor VR1 ligands I [R1 = H, OH, halo, (un)substituted alkyl, alkoxy, fluoroalkyl, fluoroalkoxy, alkylthio, cycloalkyl, cycloalkoxy, or Ph, NO2, (di)(alkyl)amino, cycloalkylamino, cyano, CO2H, alkoxycarbonyl, aroyl, carbamoyl, amidino, etc.; n = 1-3; m = 0-3; R2 = H, OH, alkyl, alkenyl, alkylidenyl, alkylidynyl, F, Cl, cycloalkyl, (un)substituted Ph, naphthyl, OPh, or heteroaryl; L = bond, alkanediyl, alkenediyl, alkynediyl, cycloalkanediyl; R3 = (un)substituted Ph, naphthyl, or heteroaryl; R4, R5 = H, alkyl; X = O, S; including enantiomers, diastereomers, tautomers, solvates, and/or pharmaceutically acceptable salts]. More particularly, the invention relates to β-aminotetralin-derived ureas that are potent antagonists or agonists of VR1, and which are useful for the treatment and prevention of inflammatory and other pain conditions in mammals. Approx. 120 compds. were prepared, and these plus addnl. compds. are claimed individually. Claims also relate to pharmaceutical compns., methods of treatment, and kits for treatment of a long list of diseases and conditions. For example, condensation of isoquinolin-5-ylcarbamic acid Ph ester with 1-benzyl-6-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamine HCl in DMSO in the presence of DIPEA at room temperature gave invention compound II. This compound inhibited binding of [3H]-RTX to recombinant human VR1 receptors in vitro with a Ki value of 3.37 nM. In functional expts., II blocked the activation of human recombinant VR1 elicited by agonists including low pH, PMA-induced PKC phosphorylation, anandamide, H2O2, and DTT; the potency was comparable to capsazepine. Compds. I also inhibited capsaicin-induced

currents in dissociated rat DRG neurons. II potently antagonized capsaicin-induced contraction of isolated guinea pig bronchial rings, with an estimated pA2 of 8.0±0.02.

IT 628720-97-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aminotetralin-derived ureas as vanilloid VR1 receptor modulators)

RN 628720-97-8 CA

CN Urea, N-[6-fluoro-1,2,3,4-tetrahydro-1-(phenylmethyl)-2-naphthalenyl]-N'-(3-hydroxy-5-quinolinyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file marpat

=> s l1 full
L8 14 SEA SSS FUL L1

=> s l2 full
L9 1 SEA SSS FUL L2

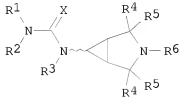
=> d l8 ibib abs fqhit 1-14

L8 ANSWER 1 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 148:191837 MARPAT
TITLE: 3-Azabicyclo[3.1.0]hexane derivatives as vanilloid receptor ligands, pharmaceutical compositions containing them and process for their preparation
INVENTOR(S): Gharat, Laxmikant Atmaram; Joshi, Neelima Khairatkar; Gajera, Jitendra Maganbhai; Yadav, Pravin Sabhajit
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals S.A., Switz.
SOURCE: PCT Int. Appl., 116pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2008010061 A2 20080124 WO 2007-IB2002 20070716
WO 2008010061 A3 20080417
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRIORITY APPLN. INFO.: IN 2006-MU1136 20060717
US 2006-835560P 20060803
IN 2007-MU381 20070227
US 2007-893675P 20070308
US 2007-947715P 20070703

GI



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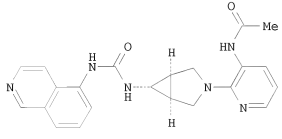


II

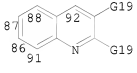
AB The invention relates to substituted 3-azabicyclo[3.1.0]hexane derivs., which are useful as vanilloid receptor ligands, methods of treating diseases, conditions and/or disorders modulated by vanilloid receptors with them, and processes for preparing them. Compds. of formula I wherein X is O and S; R1 is quinolinyl, isoquinolinyl, 2-oxodihydroquinolinyl, and 1-oxodihydroisoquinolinyl; R2 and R3 are independently H, OH, and C1-6 alkyl; R4 and R5 are independently H, halo and alkyl; R4R5 taken together to form =O and =S; R6 is H, NO2, CN, CHO, Ac, halo, OH and derivs., SH and derivs., (un)substituted alkyl, (un)substituted (hetero)aryl, etc.; and their prodrugs, pharmaceutically acceptable salts, N-oxides, esters, solvates, tautomers, stereoisomers and polymorphs thereof, are claimed.

Example compound II was prepared by a general procedure (procedure given). All the invention compds. were evaluated for their TRPV1 inhibitory activity (data given).

MSTR 1

G1 = O
G2 = 13

G4 = NH
G18 = 88-10 91-52 86-53 87-54 92-55



G19 = OH (opt. substd.)
G28 = 677

Patent location: claim 1
Note: additional derivatization also claimed
Note: or prodrugs, pharmaceutically acceptable salts, N-oxides, esters, solvates, tautomers or polymorphs
Note: also incorporates claim 43, structure 7 and claim 46, structure 8b
Stereochemistry: or stereoisomers

L8 ANSWER 2 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 146:100694 MARPAT
TITLE: Preparation of piperidine derivatives as NMDA receptor

antagonists
INVENTOR(S): Masui, Moriyasu; Matsumura, Akira
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 111pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006137465	A1	20061228	WO 2006-JP312466	20060622

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

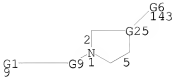
PRIORITY APPLN. INFO.: JP 2005-185100 20050624
JP 2005-309760 20051025

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [A1 = nitrogenated aromatic monocyclic group or nitrogenated aromatic fused-ring group which has at least one (un)protected hydroxy and/or amino and which may be substituted by other group, nitrogenated aromatic monocyclic group or nitrogenated aromatic fused-ring group which has -NH- in the ring and in which other ring-constituting atom may have substituent(s) (except (un)protected hydroxy and amino); A2 = (un)substituted aromatic cyclic hydrocarbon, (un)substituted aromatic heterocycle; R1 = H, hydroxy, acyloxy, etc.; R2 = H, hydroxy, alkyl; R1 and R2 may combine to form single bond; m = 0, 1; X = (un)substituted alkenylene, (un)substituted alkynylene, -CO(CR3R4)n-, etc.; R3, R4 = H, (un)substituted alkyl; n = 0-4; when m is 0, Y represents single bond, -O-, -S-, etc.; when m is 1, Y represents single bond, alkylene, alkenylene, etc.], pharmaceutically acceptable salts or solvates thereof were prepared For example, EDCI mediated amidation of 4-imidazolecarboxylic acid with compound II, e.g., prepared from 4-(4-chlorophenyl)-1,2,3,6-tetrahydropyridine hydrochloride in 2 steps, afforded compound III [R = imidazol-4-yl] in 35% yield. In NMDA receptor (NR1/NR2B receptor) binding assays, the IC50 value of compound III [R = 2,3-dihydro-2-oxo-1H-benzimidazol-5-yl] was 0.002 μM. Compds. I are claimed useful as analgesics.

MSTR 1



G1 = quinolinyl (substd. by OH)
G9 = 27-9 29-1

G10 = NH
G22 = bond
G25 = 3-2 4-5 17-143

Patent location: claim 1
Note: substitution is restricted
Note: or pharmaceutically acceptable salts or solvates

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 142:463618 MARPAT
TITLE: Preparation of 1,2,3,4-tetrahydroquinolinylurea derivatives as vanilloid receptor antagonists
INVENTOR(S): Bouchon, Axel; Diedrichs, Nicole; Hermann, Achim; Lustig, Klemens; Meier, Heinrich; Pernerstorfer, Josef; Reissmueller, Elke; Mogi, Muneto; Fujishima, Hiroshi; Tajimi, Masaomi; Yamamoto, Noriyuki
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005044802	A2	20050519	WO 2004-EP12051	20041026

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2545109	A1	20050519	CA 2004-2545109	20041026	
EP 1685112	A2	20060802	EP 2004-790836	20041026	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
JP 2007523888	T	20070823	JP 2006-538691	20041026	
US 20070213363	A1	20070913	US 2006-578413	20060505	
PRIORITY APPLN. INFO.:			EP 2003-25575	20031108	
			WO 2004-EP12051	20041026	

OTHER SOURCE(S): CASREACT 142:463618

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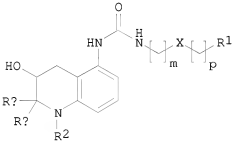
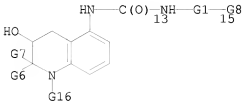


I

AB This invention relates to 1,2,3,4-tetrahydroquinolinylurea derivs. (I) and salts thereof [wherein m, p = 0-3; X = bond, O, N(R10) (wherein R10 = H, C1-6 alkyl); with the proviso that when m = 0, then X = a bond; RA = RB = H, or RA and RB together form a carbonylgroup with the carbon-atom to which they are connected; R1 = each (un)substituted aryl or heteroaryl; R2 = C1-6 alkylcarbonyl, C1-6 alkylsulfonyl, H, HO, aryl, heteroaryl, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, arylsulfonyl, or heteroaryl sulfonyl, wherein said alkyl, alkenyl or alkynyl are optionally substituted] which are useful as active ingredients of pharmaceutical prepns. The 1,2,3,4-tetrahydroquinolinylurea derivs. of the present invention have vanilloid receptor (VR1) antagonistic activity (no data). These compds. can be used for the prophylaxis and treatment of diseases associated with VR1 activity, in particular for the treatment of urol. diseases or disorders, such as detrusor overactivity (overactive bladder), urinary incontinence, neurogenic detrusor overactivity (detrusor hyperflexia), idiopathic detrusor overactivity (detrusor instability), benign prostatic hyperplasia, and lower urinary tract symptoms; pain such as chronic pain, neuropathic pain, postoperative pain, rheumatoid arthritic pain, neuralgia, neuropathies, algesia, nerve injury, ischemia, neurodegeneration, and stroke; and inflammatory disorders such as asthma and chronic obstructive pulmonary (or airways) disease (COPD). Thus, 5-amino-3-hydroxy-3,4-dihydroquinolin-2(1H)-one > (300 mg, 1.68 mmol) was dissolved in EtOAc and cooled to 0° and 4-trifluoromethylbenzyl isocyanate (339 mg, 1.68 mmol) was added slowly with stirring. The reaction mixture was stirred for 1 h at room temperature and the insol. product

was filtered and dried in vacuo to give 16% N-(3-Hydroxy-2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)-N'-[4-(trifluoromethyl)benzyl]urea (103 mg).

MSTR 1



G1 = bond
G8 = Ph (opt. substd. by 1 or more G21)
Patent location: claim 1
Note: or salts
Stereochemistry: or stereoisomeric forms

L8 ANSWER 4 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 139:364692 MARPAT
TITLE: Preparation of substituted phenyl compounds for the treatment of non-insulin dependent diabetes mellitus
INVENTOR(S): Sabatucci, Joseph P.; Caufield, Craig E.; Greenfield, Alexander A.; Morris, Koi M.; Morrison, Eamonn P.
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030203941	A1	20031030	US 2003-408912	20030408
US 6930131	B2	20050816		
PRIORITY APPLN. INFO.:			US 2002-371540P	20020410

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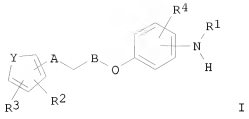
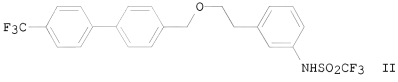


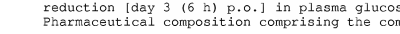
I



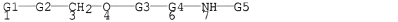
II

AB The title compds. [I; Y = O, S, N, C:C, C:N; R1 = SO2CF3, SO2Ar, SO2Me, CONH2, etc.; Ar = (un)substituted Ph, naphthyl, quinolyl; R2, R3 = H, halo, OH, etc.; R4 = H, halo, alkoxy; A = a bond, divalent group such as (un)substituted imidazole, thiazole, oxazole, etc.; B = CH2, CH2CHR5, CHR5CH2, CHR9R10; R5, R9, R10 = alkyl, F, H] that are useful in treating metabolic disorders mediated by insulin resistance or hyperglycemia, were prepared E.g., a 3-step synthesis of II (starting from 3-(2-hydroxyethyl)phenylamine and 4-bromobenzyl chloride) which showed 34% reduction [day 3 (6 h) p.o.] in plasma glucose at 5 mg/kg, was given. Pharmaceutical composition comprising the compound I is claimed.

MSTR 1



G2 = bond
G4 = phenylene (opt. substd. by 1 or more G11)
G5 = 9



G12 = 11-7 12-10

G13 = quinolinyl (opt. substd. by (1-2) G14)
G14 = OH
Patent location: claim 1
Note: or pharmaceutically acceptable salts

L8 ANSWER 5 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 139:292162 MARPAT
TITLE: Heteroaromatic ureas as vanilloid receptor (VR1) modulators, in particular antagonists, for treating pain and/or inflammation
INVENTOR(S): Brown, Rebecca Elizabeth; Doughty, Victoria Alexandra; Hollingworth, Gregory John; Jones, A. Brian; Lindon, Matthew John; Moyes, Christopher Richard; Rogers, Lauren
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080578	A1	20031002	WO 2003-GB1302	20030321
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479150	A1	20031002	CA 2003-2479150	20030321
AU 2003214442	A1	20031008	AU 2003-214442	20030321
EP 1490340	A1	20041229	EP 2003-710014	20030321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005526798	T	20050908	JP 2003-578333	20030321
US 20050107388	A1	20050519	US 2004-505358	20040819
US 7285563	B2	20071023		
PRIORITY APPLN. INFO.:			GB 2002-6876	20020322
			WO 2003-GB1302	20030321

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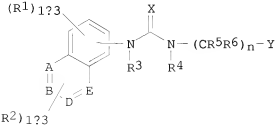
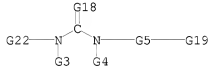


I

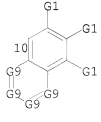
AB Title compds. I [wherein A, B, D, E are each C or N with the proviso that one or more are N; R1, R2 = independently H, halo, alk(enyl/ynyl), haloalkyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, NH2 and derivs., CO2H and derivs., (un)substituted alkyl, alkoxy; R3, R4 = independently H, alk(en/yn)yl; R5, R6 = at each occurrence, independently H, alk(enyl/ynyl), alkoxy, acyloxy, carboxy and derivs., CONH2 and derivs., sulfonyl(alkyl/amino), aryl, hetero(aryl/cyclyl), (un)substituted alkyl; or CR5R6 = 3-6 carbocyclic membered ring; R7, R8 = at each occurrence, independently H, alk(en/yn)yl, cycloalkyl, fluoroalkyl; or NR7R8 = (un)substituted 4-7 heteroaliph. membered ring; X = O, S or =NCN; Y = aryl, heteroaryl, carbocyclyl, fused carbocyclyl group; n = 0, 1, 2, 3; and their pharmaceutically acceptable salts, N-oxides, and prodrugs] were prepared as vanilloid receptor (VR1) modulators, in particular antagonists, for treating conditions or diseases in which pain and/or inflammation predominates. For example, 1-isoquinolin-5-yl-3-(3-phenylpropyl)urea was prepared by reacting isoquinoline-5-carboxylic acid with diphenylphosphoryl azide in toluene at reflux for 1 h through a Curtius rearrangement, followed by addition of 3-phenylpropylamine and reflux for 18 h. I bound to the VR1 receptor with an IC50 < 1 μM, and in the majority of cases, < 200 nM. I are predominantly VR1 antagonists with a few of them VR1 partial antagonists and VR1 partial agonists. Thus, I and their pharmaceutical compns. are useful for treating pain and/or inflammation.

MSTR 1



G2 = OH
G5 = G21
G9 = (1-3) N / 28

G18 = O
G19 = Ph (opt. substd. by 1 or more G24)
G21 = (0-3) CH2 (opt. substd.)
G22 = 10



Patent location: claim 1
Note: substitution is restricted
Note: or pharmaceutically acceptable salts, N- or S-oxides, or prodrugs
Note: additional ring formation also claimed

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 138:271682 MARPAT
TITLE: Preparation of cyclic hydroxamic acids as inhibitors of matrix metalloproteinases and/or TNF-α converting enzyme for treatment of inflammatory disorders
INVENTOR(S): Ott, Gregory; Chen, Xiao-Tao; Duan, Jingwu; Lu, Zhonghui
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 344 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024899	A2	20030327	WO 2002-US29685	20020916
WO 2003024899	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002341715	A1	20030401	AU 2002-341715	20020916
US 20030139388	A1	20030724	US 2002-244626	20020916
US 6740649	B2	20040525		
EP 1427408	A2	20040616	EP 2002-775865	20020916
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:			US 2001-322630P	20010917
			WO 2002-US29685	20020916

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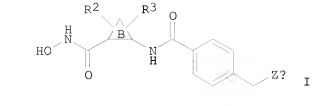

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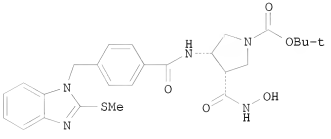
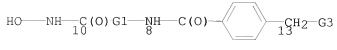


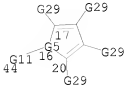
II

AB Title compds. I [wherein ring B = (un)substituted 4-7 membered (hetero)cyclic ring containing 0-2 O, N, NR1, or SOp atoms and 0-3 carbonyl groups; R1 and R2 = independently Q, alk(en/yn)ylene-Q, or (un)substituted alkylene-Q interrupted by O, NRa, CO, CO2, CONRa, NRaCO, NRaCO2, NRaCONRa, SOp, NRaSO2, or SO2NRa; or R1 = (un)substituted alkylene-Q interrupted by OCO, OCO2, or OCONRa; Q = H or (un)substituted (hetero)cyclyl; R3 = Q1, Cl, F, alk(en/yn)ylene-Q1, or (un)substituted alkylene-Q1 interrupted by O, NR1, NRaCO, CONRa, CO, CO2, SOp, or SO2NRa; Q1 = H or (un)substituted Ph, naphthyl, or heterocyclyl; Za = (un)substituted benzimidazolyl, indolyl, imidazopyridinyl, pyrazolylpyridinyl, benzofuranyl, benzothiazinyl, quinolinyl, etc.; Ra = independently H, alkyl, Ph, or benzyl; p = 0-2; or stereoisomers or pharmaceutically acceptable salts thereof] were prepared as inhibitors of matrix metalloproteinases (MMP), TNF-a converting enzyme (TACE), aggrecanase, or a combination thereof. For example, reaction of benzyl Me maleate with paraformaldehyde and glycine gave benzyl Me (cis)-3,4-pyrrolidinedicarboxlyate (100%). BOC-protection (64%), debenzylation (96%), resolution of the (3S,4S)-isomer with (S)-α-methylbenzylamine, conversion to the carbamate with DPPA and PhCH2OH (76%), and Pd catalyzed hydrogenation (100%) provided Me (3S,4S)-4-amino-1-(tert-butoxycarbonyl)-3-pyrrolidinecarboxylate. Coupling of the amine with 4-[(2-methylthio-1H-benzimidazol-1-yl)methyl]benzoic acid (preparation given) afforded the amide (99%), which was treated with NH2OH•HCl/MeONa to give the hydroxamic acid (3S,4S)-II (33%). A number of the compds. of the invention inhibited MMP-1, 2, 3, 7, 8, 9, 10, 12, 13, 14, 15, and/or 16 with Ki values of ≤ 10 μM. Thus, I are useful for the treatment of a wide variety of inflammatory disorders (no data).

MSTR 1



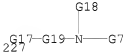
G3 = 16



G5 = 80-13 78-44 81-17 82-20

G7 = Ph
G11 = OH
G17 = 121

G19 = C(O)
G29 = 227



Patent location: claim 1
Note: or pharmaceutically acceptable salts
Note: substitution is restricted
Note: additional ring formation also claimed
Stereochemistry: or stereoisomers

L8 ANSWER 7 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 135:303914 MARPAT
TITLE: Preparation of compounds which contain a 1,2,4-trioxane moiety linked to a quinoline moiety for pharmaceutical use as antimalarial agents
INVENTOR(S): Meunier, Bernard; Robert, Anne; Dechy-Cabaret, Odile; Benoit-Vical, Francoise
PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique (C.N.R.S.), Fr.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077105	A1	20011018	WO 2001-FR1013	20010404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2807433	A1	20011012	FR 2000-4422	20000406
FR 2807433	B1	20020920		
CA 2405076	A1	20011018	CA 2001-2405076	20010404
EP 1268470	A1	20030102	EP 2001-921476	20010404
EP 1268470	B1	20080227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001009885	A	20030603	BR 2001-9885	20010404
HU 2003000428	A2	20030628	HU 2003-428	20010404
JP 2004521855	T	20040722	JP 2001-575578	20010404
AP 1399	A	20050427	AP 2002-2646	20010404
NZ 521774	A	20051028	NZ 2001-521774	20010404
AU 2001248463	B2	20060316	AU 2001-248463	20010404
AT 387441	T	20080315	AT 2001-921476	20010404
ES 2302727	T3	20080801	ES 2001-921476	20010404
ZA 2002007851	A	20040126	ZA 2002-7851	20020930
IN 2002MN01348	A	20040703	IN 2002-MN1348	20020930
NO 2002004795	A	20021206	NO 2002-4795	20021004
MX 2002PA09856	A	20040226	MX 2002-PA9856	20021004
KR 832047	B1	20080527	KR 2002-713363	20021005
US 20040038957	A1	20040226	US 2003-240929	20030204
US 6949569	B2	20050927		
HK 1056882	A1	20051014	HK 2003-109287	20040106
US 20050288315	A1	20051229	US 2005-196979	20050804

PRIORITY APPLN. INFO.:

FR 2000-4422		20000406
WO 2001-FR1013		20010404
US 2003-240929		20030204

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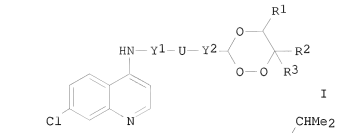

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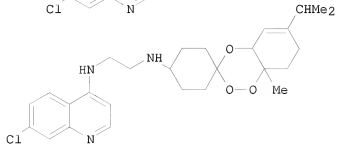


II

AB 1,2,4-Trioxanes, such as I [R1, R2 = H, fused carbocyclic ring, alkyl, etc.; R3 = H, Me, Ph, etc.; Y1, Y2 = linking group, such as alkylene, cycloalkylene; U = O, S, amino, amide sulfonamide, carboxy, etc.], were prepared for use a therapeutic agents for the treatment of malaria. Thus, trioxane II as its dicitrate salt, designated as DU 1302, was prepared via cyclization of α-terpinene and 1,4-cyclohexanedione by photooxidn. using oxygen in CH2Cl2 followed by condensation of the resulting keto-trioxane with N-(7-chloro-4-quinolinyl)-1,2-ethanediamine using sodium triacetoxyborohydride in CH2Cl2. The prepared trioxanes were tested for antimalarial activity against three strains of Plasmodium falciparum, i.e. FcB1-Columbia, FcM29-Cameroon, and Nigerian. Also, pharmaceutical compns. of the trioxanes were presented.

MSTR 1A

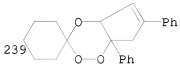
G1 = 40

G2 = 4-1 6-3 / 25-1 26-3

G3 = alkylene <containing 1 or more C>
(opt. substd. by 1 or more OH)
G5 = NH (opt. substd.)

G7 = 27-1 28-26

G8 = 239



G14 = NH
G16 = quinolinyl (opt. substd. by 1 or more G17)
G17 = OH
Patent location: claim 1
Note: additional interruptions in G3 alkylene chains also claimed
Note: additional ring formation also claimed
Note: and pharmaceutically acceptable acid addition salts
Note: substitution is restricted

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 127:205815 MARPAT
TITLE: Preparation of sialyl-Lewisa and sialyl-Lewisx epitope analogs as E-selection receptors
INVENTOR(S): Oehrlein, Reinhold
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Oehrlein, Reinhold
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9728174	A1	19970807	WO 1997-EP223	19970117
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9714446	A	19970822	AU 1997-14446	19970117
EP 886639	A1	19981230	EP 1997-901068	19970117
EP 886639	B1	20080528		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 397005	T	20080615	AT 1997-901068	19970117
US 6187754	B1	20010213	US 1999-117521	19990108

PRIORITY APPLN. INFO.: CH 1996-229 19960130
WO 1997-EP223 19970117

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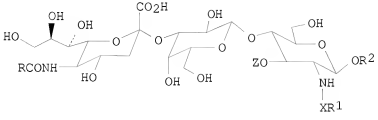
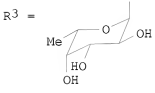
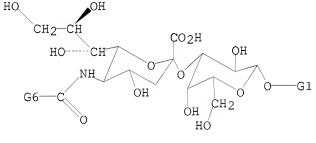




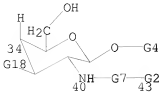
I

AB Sialyl-Lewisa and sialyl-Lewisx epitope analogs I (Z = α-pyranose; R1 = H, alkyl, alkenyl, cycloalkyl, heteroaryl, cycloaryl; R2 = alkyl, cycloalkyl; R3 = Me, hydroxymethyl; X = CO, CS, SO2, acyl, thiocarbonyl) in which the naturally occurring N-acetyl group of the N-acetylglucosamine monomer is replaced by various aliphatic or aromatic substituents and the L-fucose naturally present is replaced by various naturally occurring or non-naturally occurring sugars were prepared as E-selectin receptors. Thus, I (R = Me, R1 = 2-hydroxy-5-fluorophenyl, X = CO, R2 = (CH2)8CO2Me, Z = R3) was prepared and tested as E-selectin receptor (relative IC50 to an internal control is 0.039).

MSTR 1



G1 = 34



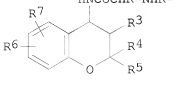
G2 = quinolinyl (substd. by 1 or more G14)
G7 = 96-40 97-43

G8 = O
G9 = NH
G14 = 1 or more OH
Patent location: claim 1
Note: substitution is restricted
Note: CH2 groups at G4 may be replace oxygen, sulfur, or an imino group
Note: also incorporates claim 32, 34, structures VII, and VIII

L8 ANSWER 9 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 126:277766 MARPAT
TITLE: Phenylglycine and phenylalanine amido benzopyran derivatives
INVENTOR(S): Atwal, Karnail S.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5612370	A	19970318	US 1995-484765	19950607

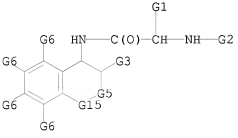
PRIORITY APPLN. INFO.: US 1995-484765 19950607
GI



I

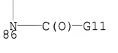
AB Title phenylglycine and phenylalanine derivs. I (R1 = aryl, arylalkyl, heterocyclyl, heterocyclylalkyl; R2 = H, alkyl, acyl, alkyl- or arylsulfonyl, etc.; R3 = H, OH, acyloxy, etc.; R4, R5 = H, alkyl, arylalkyl or CR4R5 = 5- to 7-membered carbocycle; R6 = H, alkyl, haloalkyl, alkenyl, alkynyl, etc.; R7 = H, alkyl, halo, OH, alkoxy, amino, etc.) and their pharmaceutically acceptable salts were prepared These compds. have potassium channel activating activity and are useful, e.g., as cardiovascular agents. Thus, (3S-trans)-[2-[(6-cyano-3,4-dihydro-3-hydroxy-2,2-dimethyl-2H-1-benzopyran-4-yl)amino]-2-oxo-1-phenylethyl]carbamic acid tert-Bu ester was prepared by coupling Boc-D-phenylalanine with (3S-trans)-4-amino-3,4-dihydro-3-hydroxy-2,2-dimethyl-2H-1-benzopyran-6-carbonitrile mesylate using 1-hydroxybenzotriazole and dicyclohexylcarbodiimide in DMF.

MSTR 2A



G3 = OH
G5 = 39

G6 = (up to 1) G7
G7 = 86



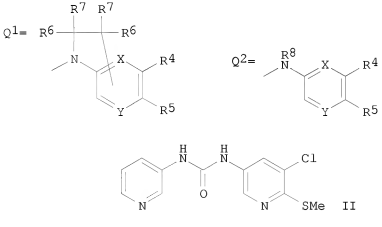
G10 = Ph
G11 = 30

G15 = NH
Derivative: or pharmaceutically acceptable salts
Patent location: disclosure

L8 ANSWER 10 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 125:114487 MARPAT
TITLE: CNS-Active pyridinylurea derivatives
INVENTOR(S): Forbes, Ian Thomson; Jones, Graham Elgin
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611930	A1	19960425	WO 1995-EP3944	19951005
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 788499	A1	19970813	EP 1995-934135	19951005
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL, SE				
JP 10508584	T	19980825	JP 1995-512907	19951005
US 5866586	A	19990202	US 1997-817580	19970417
PRIORITY APPLN. INFO.:			GB 1994-20999	19941018
			WO 1995-EP3944	19951005

GI



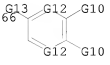
AB The invention relates to heterocyclic compds. R1-G-N(R2)-CO-R3 [I; G = Ph ring, quinoline or isoquinoline nucleus, or a 5- or 6-membered aromatic heterocycle containing 1-3 heteroatoms (N, O, and/or S); R1 = H, alkyl, alkylthio, cyano, NO2, halo, CF3, amino, etc.; R2 = H, alkyl; R3 = group Q1 or Q2; X = Y = N, or one of X and Y = N and the other = C or CH; R4, R5 = alkyl, alkoxy, OH, halo, NO2, (un)substituted Ph, etc.; or R4R5 forms (un)substituted 5-membered carbo- or heterocyclic ring; R6, R7, R8 = H, alkyl]. Compds. I are 5-HT2C receptor antagonists, and some or all of

them are also 5-HT2B antagonists. They are useful in the treatment of a variety of CNS and GI disorders. For example, 5,6-dichloronicotinic acid underwent sulfurization in the 6-position by thiourea (87%) and S,O-dimethylation with MeI (50%) to give Me 3-chloro-2-(methylthio)pyridine-5-carboxylate. This was converted to the corresponding hydrazide (32%) and then the carbonyl azide (72%). The latter was decomposed in refluxing PhMe, and the intermediate isocyanate treated with 3-aminopyridine, to give 85% title compound II. The three example compds. had pKi of 7.4-8.1 in a test for displacement of [3H]-mesulergine from rat or human 5-HT2C clones, expressed in 293 cells in vitro.

MSTR 1

G1—G6—C(O)G8

G1 = quinolinyl (opt. substd. by (1) G2)
G2 = OH
G6 = NH
G8 = 66



G12 = (up to 1) CH
G13 = NH
Derivative: or salts
Patent location: claim 1
Note: additional ring formation specified

L8 ANSWER 11 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 122:72046 MARPAT
TITLE: Medicaments for treatment of migraine, epilepsy and feeding disorders
INVENTOR(S): Blackburn, Thomas Paul; Kennett, Guy Anthony; Baxter, Gordon Smith
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9425012	A2	19941110	WO 1994-EP1240	19940420
WO 9425012	A3	19941222		

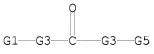
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

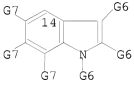
AU 9465697	A	19941121	AU 1994-65697	19940420
ZA 9402809	A	19951023	ZA 1994-2809	19940422
PRIORITY APPLN. INFO.:			GB 1993-8802	19930428
			WO 1994-EP1240	19940420

AB Indoles such as 1-[5-(2-thienylmethoxy)-1H-indol-3-yl]propan-2-amine are used in the treatment and prevention of epilepsy and migraine.

MSTR 1



G1 = quinolinyl (opt. substd. by (1) G2)
G2 = OH
G3 = NH
G5 = 14



Derivative: or pharmaceutically acceptable salts
Patent location: claim 2
Note: substitution is restricted

L8 ANSWER 12 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 121:255671 MARPAT
TITLE: Preparation of N-phenyl-N'-heteroarylureas as 5HT2C receptor antagonists
INVENTOR(S): Forbes, Ian Thomson; Ham, Peter; Roger Thomas; Thompson, Mervyn
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9418170	A1	19940818	WO 1994-EP189	19940125
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 682656	A1	19951122	EP 1994-905697	19940125
R: BE, CH, DE, FR, GB, IT, LI, NL				
JP 08506114	T	19960702	JP 1994-517583	19940125

PRIORITY APPLN. INFO.: GB 1993-2275 19930205
WO 1994-EP189 19940125

AB R1NR2CONR3R4 [R1 = (un)substituted (iso)quinolinyl, -heteroaryl; R2,R3 = H, alkyl; R4 = (un)substituted Ph] were prepared Thus, nicotinoyl azide was refluxed in PhMe after which 3,4-ClMeC6H3NH2 was added to give, after acidification, 3,4-ClMeC6H3NHCONHR1.HCl (R1 = 3-pyridyl) which had ID50 of 78mg/kg orally against mCPP-induced hypolocomotion in rats.

MSTR 1

G1—G5—C(O)G5—G6

G1 = quinolinyl (opt. substd. by (1) G2)
G2 = OH
G5 = NH
G6 = Ph (opt. substd. by (1-3) G7)
Derivative: or salts
Patent location: claim 1

L8 ANSWER 13 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 121:179617 MARPAT
TITLE: Heteroaryl Ureas as 5-HT2c and 5-HT2b Antagonists
INVENTOR(S): Forbes, Ian Thomson; Martin, Roger Thomas; Jones, Graham Elgin
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9414801	A1	19940707	WO 1993-EP3666	19931221

W: JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: GB 1992-27048 19921229
GB 1993-4414 19930304
GB 1993-6459 19930329

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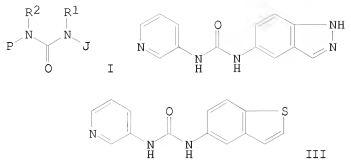
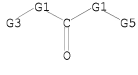


AB Heterocyclic urea derivs. I (P = quinolinyl, isoquinolinyl, heteroaryl, etc.; J = quinolinyl, tetrahydroquinolinyl, indolinyl, indazolyl, benzothienyl, etc.; R1 = H, alkyl, etc.; R2 = H, alkyl) were disclosed. I were claimed for the manufacture of antidepressants, anxiolytics, for the treatment of Alzheimer's disease, bulimia, obsessive-compulsive disorders, schizophrenia, etc. I are 5-HT2c or 5-HT2b antagonists. Specifically claimed example compds. are N-(5-Benzo[b]thienyl)-N'-(3-pyridinyl)urea (II) and N-(1-Methyl-5-indazolyl)-N'-(3-pyridinyl)urea (III).

MSTR 1



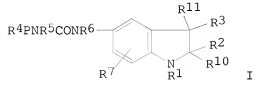
G1 = NH
G3 = quinolinyl (opt. substd. by (1) G4)
G4 = OH
G5 = quinolinyl (opt. substd. by (1-2) G6)
Derivative: or salts
Patent location: claim 1
Note: substitution is restricted

L8 ANSWER 14 OF 14 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 120:77171 MARPAT
TITLE: Preparation of indolylurea derivatives as antagonists
INVENTOR(S): Forbes, Ian Thomson; Martin, Roger Thomas; Jones, Graham Elgin
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9318028	A1	19930916	WO 1993-GB449	19930304
W: AU, CA, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9336411	A	19931005	AU 1993-36411	19930304
EP 630373	A1	19941228	EP 1993-905507	19930304
R: BE, CH, DE, FR, GB, IT, LI, NL				
JP 07504429	T	19950518	JP 1993-515449	19930304
ZA 9301713	A	19940922	ZA 1993-1713	19930310
US 5508288	A	19960416	US 1994-295694	19940830
PRIORITY APPLN. INFO.:			GB 1992-5415	19920312
			GB 1992-5416	19920312
			GB 1992-5422	19920312
			GB 1992-5442	19920312
			WO 1993-GB449	19930304

GI



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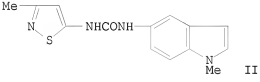
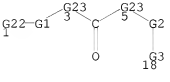


II

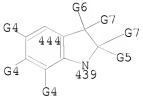
AB Title compds. I (P = quinolinyl, isoquinolyl, 5,6-membered heterocyclyl; R1 = H, C1-6 alkyl; R2, R3, R10, R11 = C2-6 alkylene; R4 = H, C1-6 alkyl, halo, R8R9N, R12O, R12O2C wherein R8, R9, R12 = H, C1-6 alkyl; R5, R6 = H, C1-6 alkyl; R7 = H, C1-6 alkyl, C1-6 alkoxy, halo; etc.) or a salt thereof, are prepared to NaH was added 5-amino-3-methylbisthiazole-HCl followed by N-(1-methyl-5-indolyl)carbamate (preparation given) to give the title compound II. The affinity of II for 5-HT1C binding site by assessing its ability to displace [3H]-mesulergine from 5-HT1C binding sites was shown by pA2 as 7.9.

MSTR 1A



G1 = 357-1 354-3

G2 = 444-5 439-18



G22 = OH
G23 = NH
Derivative: or salts or N-oxides
Patent location: claim 1

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(FILE 'HOME' ENTERED AT 10:32:09 ON 23 SEP 2008)

FILE 'REGISTRY' ENTERED AT 10:32:28 ON 23 SEP 2008
L1 STRUCTURE UPLOADED
L2 STRUCTURE UPLOADED
L3 0 S L1 SAM
L4 1 S L2 SAM
L5 29 S L1 OR L2 FULL

FILE 'CA' ENTERED AT 10:34:14 ON 23 SEP 2008
L6 2 S L5

FILE 'MARPAT' ENTERED AT 10:35:13 ON 23 SEP 2008
L7 1 S L1
L8 14 S L1 FULL
L9 1 S L2 FULL

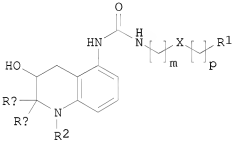
=> d l9 ibib abs fqhit

L9 ANSWER 1 OF 1 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 142:463618 MARPAT
TITLE: Preparation of 1,2,3,4-tetrahydroquinolinylurea derivatives as vanilloid receptor antagonists
INVENTOR(S): Bouchon, Axel; Diedrichs, Nicole; Hermann, Achim; Lustig, Klemens; Meier, Heinrich; Pernerstorfer, Josef; Reissmueller, Elke; Mogi, Muneto; Fujishima, Hiroshi; Tajimi, Masaomi; Yamamoto, Noriyuki
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005044802	A2	20050519	WO 2004-EP12051	20041026
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2545109	A1	20050519	CA 2004-2545109	20041026
EP 1685112	A2	20060802	EP 2004-790836	20041026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007523888	T	20070823	JP 2006-538691	20041026
US 20070213363	A1	20070913	US 2006-578413	20060505

PRIORITY APPLN. INFO.: EP 2003-25575 20031108
WO 2004-EP12051 20041026
OTHER SOURCE(S): CASREACT 142:463618
GI

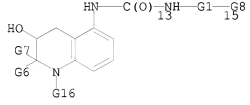


I

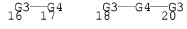
AB This invention relates to 1,2,3,4-tetrahydroquinolinylurea derivs. (I) and salts thereof [wherein m, p = 0-3; X = bond, O, N(R10) (wherein R10 = H, C1-6 alkyl); with the proviso that when m = 0, then X = a bond; RA = RB = H, or RA and RB together form a carbonylgroup with the carbon-atom to which they are connected; R1 = each (un)substituted aryl or heteroaryl; R2 = C1-6 alkylcarbonyl, C1-6 alkylsulfonyl, H, HO, aryl, heteroaryl, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, arylsulfonyl, or heteroaryl sulfonyl, wherein said alkyl, alkenyl or alkynyl are optionally substituted] which are useful as active ingredients of pharmaceutical prepns. The 1,2,3,4-tetrahydroquinolinylurea derivs. of the present

invention have vanilloid receptor (VR1) antagonistic activity (no data). These compds. can be used for the prophylaxis and treatment of diseases associated with VR1 activity, in particular for the treatment of urol. diseases or disorders, such as detrusor overactivity (overactive bladder), urinary incontinence, neurogenic detrusor overactivity (detrusor hyperflexia), idiopathic detrusor overactivity (detrusor instability), benign prostatic hyperplasia, and lower urinary tract symptoms; pain such as chronic pain, neuropathic pain, postoperative pain, rheumatoid arthritic pain, neuralgia, neuropathies, algesia, nerve injury, ischemia, neurodegeneration, and stroke; and inflammatory disorders such as asthma and chronic obstructive pulmonary (or airways) disease (COPD). Thus, 5-amino-3-hydroxy-3,4-dihydroquinolin-2(1H)-one > (300 mg, 1.68 mmol) was dissolved in EtOAc and cooled to 0° and 4-trifluoromethylbenzyl isocyanate (339 mg, 1.68 mmol) was added slowly with stirring. The reaction mixture was stirred for 1 h at room temperature and the insol. product was filtered and dried in vacuo to give 16% N-(3-Hydroxy-2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)-N'-[4-(trifluoromethyl)benzyl]urea (103 mg).

MSTR 1



G1 = 16-13 17-15 / 18-13 20-15



G3 = (1-3) CH2
G4 = O
G8 = Ph (opt. substd. by 1 or more G21)
Patent location: claim 1
Note: or salts
Stereochemistry: or stereoisomeric forms

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(FILE 'HOME' ENTERED AT 10:32:09 ON 23 SEP 2008)

FILE 'REGISTRY' ENTERED AT 10:32:28 ON 23 SEP 2008
L1 STRUCTURE UPLOADED
L2 STRUCTURE UPLOADED
L3 0 S L1 SAM
L4 1 S L2 SAM
L5 29 S L1 OR L2 FULL

FILE 'CA' ENTERED AT 10:34:14 ON 23 SEP 2008

```
L6             2 S L5

     FILE 'MARPAT' ENTERED AT 10:35:13 ON 23 SEP 2008
L7             1 S L1
L8            14 S L1 FULL
L9             1 S L2 FULL

=>

---Logging off of STN---


=>
Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 10:38:04 ON 23 SEP 2008
```